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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,937	03/22/2006	Shinya Kusuda	Q93855	5148

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EXAMINER	
LEESER, ERICH A	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
03/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,937	KUSUDA ET AL.	
	Examiner	Art Unit	
	Erich A. Leeser	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-22-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 are currently pending in the instant application. Claim 11 is cancelled.

Priority

This application is a 371 of PCT/JP04/14137, filed on 09/21/2004, which claims priority to JAPAN 2003-330616, filed on 09/22/2003 and JAPAN 2004-231546, filed on 08/06/2004.

The claimed benefit to an earlier priority date is denied as Applicant has not provided a certified translation of the priority documents. As such, the filing date of the instant application is 09/21/2004.

Information Disclosure Statement

The references disclosed in the IDS dated March 22, 2006, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claim 9 is rejected because the claim term "medicament" is confusing. Does Applicant intend this claim term to mean a pharmaceutical composition or a method for treatment? Clarification is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making solvates of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Determining if any particular substrate would form a solvate would require synthesis of the substrate and subjecting it to recrystallization with a variety of solvents, temperatures, pressures, and humidity. The experimentation is potentially open-ended. b) The direction concerning the solvates is found on pages 61-62, which simply states Applicant intends to make them. c) There is no working example of any solvate formed.

The claims are drawn to solvates, yet the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, Applicant must show that solvates can be made, or limit the claims accordingly.

d) The nature of the invention is chemical synthesis, which involves chemical reactions. e) The state of the art is that it is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). West, Anthony R., "Solid State Chemistry and its Applications, Wiley, New York, 1988, pages 358 & 365. The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further

clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air might change the stabile region of the solvate. f) The artisan using Applicant's invention to prepare the claimed compounds would be a synthetic organic chemist with a Ph.D. in organic chemistry and several years of experience. g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. h) The breadth of the claims includes all of the thousands of compounds of formula (I) as well as the presently unknown list of solvents embraced by the term "solvate".

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation would be required to practice Applicant's invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry to use the invention. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples,

d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (CCPA 1965); *In re Colianni*, 195 USPQ 150 (CCPA 1977), *Ex parte Formal*, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. First, it must itself be biologically inactive. Second, it must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation. b) The direction concerning the prodrugs in the instant application is found on page 15, lines 21-27 through page 16, lines 1-20. c) There is no working example of a prodrug of a compound of formula (I). d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. e) Wolff (Medicinal Chemistry) summarizes the state of the prodrug art. Wolff, Manfred E., *Burger's Medicinal Chemistry, 5ed., Part I*, John Wiley & Sons, pages 975-977 (1995). The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue,

the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker, G.S., et al, *Modern Pharmaceutics, 3ed.*, Marcel Dekker, New York, pages 451 & 596 (1996). In the first sentence, third paragraph on page 596 it states that "extensive development must be undertaken" to find a prodrug. f) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicant's prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. g) It is well-established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the thousands of compounds of formula (I) as well as the presently unknown list of potential prodrug derivatives embraced by claim 1.

Claims 6-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compound to treat any and all known or unknown PPAR-mediated diseases. While enabling for the PPARδ-mediated disease hyperlipidemia, the specification is insufficient to enable other diseases mediated by PPARδ other than hyperlipidemia. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of

the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention:

The instant invention is drawn to methods for treatment of PPAR-mediated diseases in a mammal or a pharmaceutical composition comprising a compound represented by formula (I).

The state of the prior art:

The state of the prior art at the time the invention was made clearly shows the level of uncertainty in the pharmacokinetic community regarding treatment of PPAR-mediated diseases: " Dyslipidaemia is a major risk factor in the development of atherosclerosis, and lipid lowering is achieved clinically using fibrate drugs and statins. Recent studies have found that PPARδ is also a regulator of serum lipids. However, *there are currently no drugs in clinical use that selectively activate this receptor.* It is clear that all three forms of PPARs have mechanistically different modes of lipid lowering and that *drugs currently available have not been optimized on the basis of PPAR biology.* Future design of drugs that have specific PPAR-activating properties may also be useful in the prevention of cardiovascular disease in a growing population suffering from lifestyle-induced metabolic dysfunction." (Emphasis added). Vosper et al., *Peroxisome proliferator-activated receptor agonists, hyperlipidaemia, and atherosclerosis*, Pharmacology & Therapeutics, Vol. 95, pages 47-62 (2002).

The predictability in the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly unpredictable since one skilled in the art would not necessarily recognize whether or not the compounds of formula (I) of claim 1 would be useful for treating a PPAR-mediated disease in a mammal.

Amount of guidance/working examples:

Applicant provides examples of the instant compounds showing superior agonistic activity against PPARδ in Table 1. Applicant has also shown the present compounds are useful as a therapeutic agent for treating hyperlipidemia in Table (2). However, Applicant provides no examples for treating or preventing PPARδ-mediated diseases using the compounds of formula (I) other than Table (1) and (2), which do not definitively prove that compounds of formula (I) treat PPARδ-mediated diseases.

The breadth of the claims:

The breadth of claims is unduly broad because one skilled in the art would not necessarily know which specific disease states are included in the claim term "PPAR-mediated disease" and which are excluded.

The quantity of undue experimentation needed:

Since the guidance and teaching provided by the specification is insufficient for treating a PPAR-mediated disease utilizing a compound of formula (I), one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art:

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, the specification is not enabled to show that compounds of formula (I) are capable of treating a PPAR-mediated disease.

Claims 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the phenylacetic acid derivative compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of

record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (CCPA 1965); *In re Colianni*, 195 USPQ 150 (CCPA 1977), *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before affliction occurs. This would require extensive and potentially open-ended clinical research on healthy subjects. 2) The passage spanning lines 10-13, page 8 lists the diseases Applicant intends to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized in treating hyperlipidemia with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of PPAR-mediated diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished. *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art.

Genentech vs. Novo Nordisk, 42 USPQ2nd 1001, 1006. 7) It is well-established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by formula (I).

The Examiner suggests deletion of the word "prevention".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

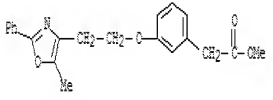
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

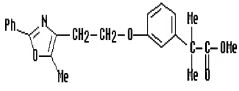
The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-2, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Tajima et al., WO 9946232. Tajima et al. discloses the instant claimed compounds and compositions, which from the STN search are:

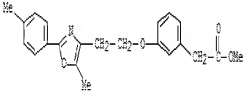
3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]-methyl ester benzeneacetic acid,



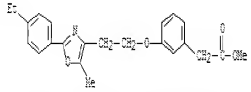
a,a-dimethyl-3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]-methyl ester benzeneacetic acid,



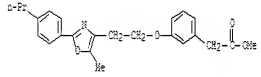
3-[2-[5-methyl-2-(4-methylphenyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



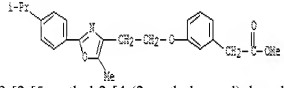
3-[2-[2-(4-ethylphenyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



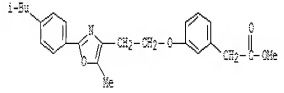
, 3-[2-[5-methyl-2-(4-propylphenyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



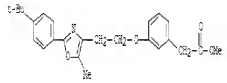
, 3-[2-[5-methyl-2-[4-(1-methylethyl)phenyl]-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



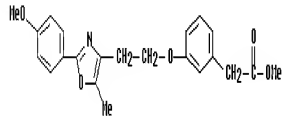
, 3-[2-[5-methyl-2-[4-(2-methylpropyl)phenyl]-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



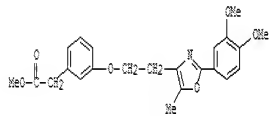
, 3-[2-[2-[4-(1,1-dimethylethyl)phenyl]-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



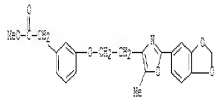
3-[2-[2-(4-methoxyphenyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



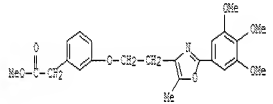
3-[2-[2-(3,4-dimethoxyphenyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



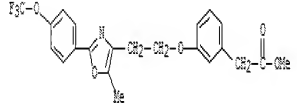
3-[2-[2-(1,3-benzodioxol-5-yl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



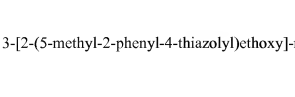
3-[2-[5-methyl-2-(3,4,5-trimethoxyphenyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



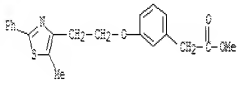
3-[2-[5-methyl-2-[4-(trifluoromethoxy)phenyl]-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



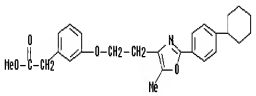
3-[2-[2-(2,2-difluoro-1,3-benzodioxol-5-yl)-5-methyl-4- oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



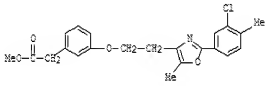
3-[2-(5-methyl-2-phenyl-4-thiazolyl)ethoxy]-methyl ester benzeneacetic acid,



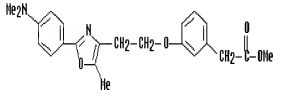
3-[2-[2-(4-cyclohexylphenyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



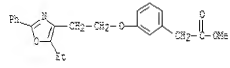
3-[2-[2-(3-chloro-4-methylphenyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



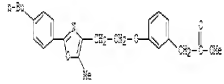
3-[2-[2-[4-(dimethylamino)phenyl]-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



3-[2-(5-ethyl-2-phenyl-4-oxazolyl)ethoxy]-methyl ester benzeneacetic acid,



3-[2-[2-(4-butylphenyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



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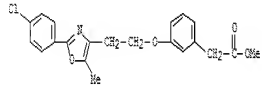

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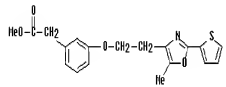
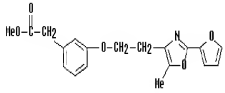
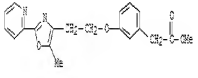


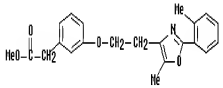
3-[2-[2-(2-furanyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



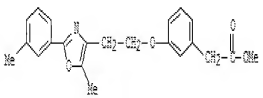
3-[2-[5-methyl-2-(2-pyridinyl)-4-oxazolyl]ethoxy]-methyl ester benzeneaccetic acid,



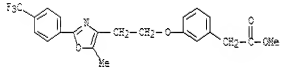
3-[2-[5-methyl-2-(2-methylphenyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



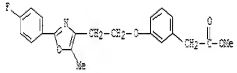
3-[2-[5-methyl-2-(3-methylphenyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



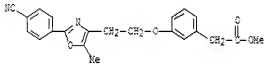
3-[2-[5-methyl-2-[4-(trifluoromethyl)phenyl]-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



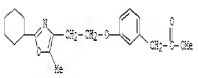
3-[2-[2-(4-fluorophenyl)-5-methyl-4-oxazolyl]ethoxy]-,methyl ester benzeneacetic acid,



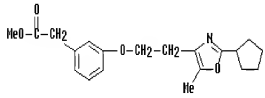
3-[2-[2-(4-cyanophenyl)-5-methyl-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



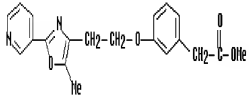
3-[2-(2-cyclohexyl-5-methyl-4-oxazolyl)ethoxy]-methyl ester benzeneacetic acid,



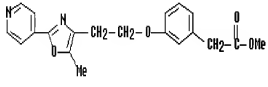
3-[2-(2-cyclopentyl-5-methyl-4-oxazolyl)ethoxy]-methyl ester benzeneacetic acid,



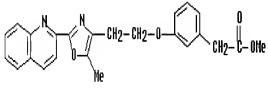
3-[2-[5-methyl-2-(3-pyridinyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



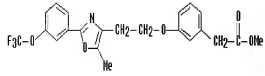
3-[2-[5-methyl-2-(4-pyridinyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



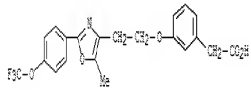
3-[2-[5-methyl-2-(2-quinolinyl)-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



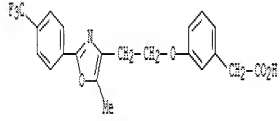
3-[2-[5-methyl-2-[3-(trifluoromethoxy)phenyl]-4-oxazolyl]ethoxy]-methyl ester benzeneacetic acid,



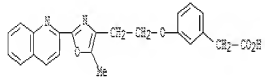
3-[2-[5-methyl-2-[4-(trifluoromethoxy)phenyl]-4-oxazolyl]ethoxy]-benzeneacetic acid,



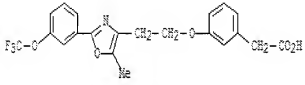
3-[2-[5-methyl-2-[4-(trifluoromethyl)phenyl]-4-oxazolyl]ethoxy]-benzeneacetic acid,



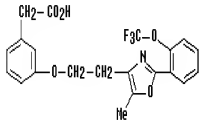
3-[2-[5-methyl-2-(2-quinolinyl)-4-oxazolyl]ethoxy]-benzeneacetic acid,



3-[2-[5-methyl-2-[3-(trifluoromethoxy)phenyl]-4-oxazolyl]ethoxy]-benzeneacetic acid,



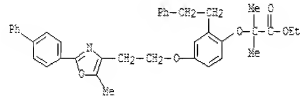
3-[2-[5-methyl-2-[2-(trifluoromethoxy)phenyl]-4-oxazolyl]ethoxy]-benzeneacetic acid,



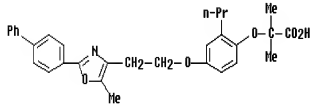
Therefore, the instant claims are anticipated by Tajima et al.

Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Brooks et al., WO 2001016120. Brooks et al. discloses the instant claimed compounds and compositions, which from the STN search are:

2-[4-[2-(2-[1,1'-biphenyl]-4-yl-5-methyl-4-oxazolyl)ethoxy]-2-(2-phenylethyl)phenoxy]-2-methyl-ethyl ester propanoic acid,



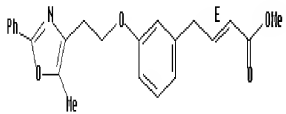
2-[4-[2-(2-[1,1'-biphenyl]-4-yl-5-methyl-4-oxazolyl)ethoxy]-2-propylphenoxy]-2-methyl-propanoic acid,



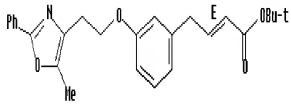
Therefore, the instant claims are anticipated by Brooks et al.

Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheng et al., WO 2002096358. Cheng et al. discloses the instant claimed compounds and compositions, which from the STN search are:

4-[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]-methyl ester, (2E)- 2-butenoic acid,



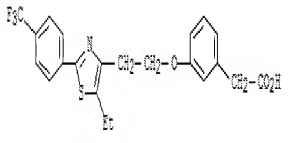
4-[3-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]-1,1-dimethylethyl ester, (2E)- 2-butenoic acid,



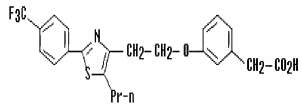
Therefore, the instant claims are anticipated by Cheng et al.

Claims 1-2, 4-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Conner et al., WO 2003072102. Conner et al. discloses the instant claimed compounds and compositions, which from the STN search are:

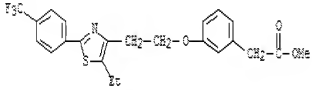
3-[2-[5-ethyl-2-[4-(trifluoromethyl)phenyl]-4-thiazolyl]ethoxy]-benzeneacetic acid,



3-[2-[5-propyl-2-[4-(trifluoromethyl)phenyl]-4-thiazolyl]ethoxy]-benzeneacetic acid,



3-[2-[5-ethyl-2-[4-(trifluoromethyl)phenyl]-4-thiazolyl]ethoxy]-methyl ester benzeneacetic acid,



Therefore, the instant claims are anticipated by Conner et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. 2. Ascertaining the differences between the prior art and the claims at issue.
3. 3. Resolving the level of ordinary skill in the pertinent art.

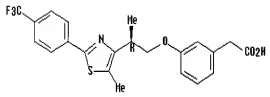
4. 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2 and 5 are rejected under 103(a) as being unpatentable over Conner et al., WO 2003072100.

Determination of the scope and content of the prior art (MPEP §2141.01)

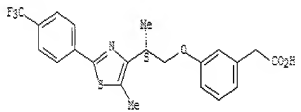
Conner et al. discloses analogous compounds, which from the STN search are:

3-[(2R)-2-[5-methyl-2-[4-(trifluoromethyl)phenyl]-4-thiazolyl]propoxy]-benzeneacetic acid,



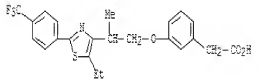
,

3-[(2S)-2-[5-methyl-2-[4-(trifluoromethyl)phenyl]-4-thiazolyl]propoxy]-benzeneacetic acid,

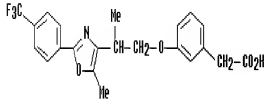


,

3-[2-[5-ethyl-2-[4-(trifluoromethyl)phenyl]-4-thiazolyl]propoxy]-benzeneacetic acid,



3-[2-[5-methyl-2-[4-(trifluoromethyl)phenyl]-4-oxazolyl]propoxy]-benzeneacetic acid,



Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compounds are that the prior art compounds replaces one hydrogen of the instant compound with a methyl.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected results, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Erich A. Leeser/

/James O. Wilson/
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Art Unit 1624

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